PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

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Weickmann & Weickmann
Patentanwälte
13. SEP. 2006
Frist:

Date of mailing *(day/month/year)* 08 September 2006 (08.09.2006)	
Applicant's or agent's file reference 27186P WO	**IMPORTANT NOTIFICATION**
International application No. PCT/EP2004/013131	International filing date *(day/month/year)* 18 November 2004 (18.11.2004)
Applicant FEBIT BIOTECH GMBH et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Ellen Moyse
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 27186P WO	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2004/013131	International filing date *(day/month/year)* 18 November 2004 (18.11.2004)	Priority date *(day/month/year)* 18 November 2003 (18.11.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant FEBIT BIOTECH GMBH		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 29 August 2006 (29.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Ellen Moyse e-mail: pt05@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	See form PCT/ISA/210
Applicant's or agent's file reference 27186P WO	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/013131	18.11.2004	18.11.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68,A61K48/00

Applicant
FEBIT BIOTECH GMBH

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP Facsimile No.	Authorized officer Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/013131

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/013131

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-31	NO
Inventive step (IS)	Claims		YES
	Claims	1-31	NO
Industrial applicability (IA)	Claims	1-31	YES
	Claims		NO

2. Citations and explanations:

Reference is made to the following documents:

D1: WO 93/17126 A (THE PUBLIC HEALTH RESEARCH INSTITUTE OF THE CITY O)5 July 2001 (2001-07-05)

D2: WO 01/48242 A (MERGEN LTD) 5 July (2001-07-05)

D3: WANG J ET AL: "DNA microarrays with unimolecular hairpin double-stranded DNA probes: Fabrication and exploration of sequence-specific DNA/protein interactions" JOURNAL OF BIOCHEMICAL AND BIOPHYSICAL METHODS, AMSTERDAM, NL, Vol. 55, No. 3, March 2003 (2003-03), pages 215-232, XP002251375 ISSN: 0165-022X

D4: WO 99/32654 A (HITACHI CHEMICAL CO. LTD. HITACHI CHEMICAL RESEARCH CENTER, INC; MITS) 1 July 1999 (1999-07-01)

D5: WO 99/05321 A (RAPIGENE, INC) 4 February 1999 (1999-02-04)

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Novelty and inventive step (PCT Article 33(2) and (3))

1.1 The present application relates to a method for manufacturing nucleic acids by
a) preparation of a carrier (array) to which different nucleic acid fragments are bound,
b) a synthesis reaction of a complementary nucleic acid strand and either

c) detachment of the nucleic acids generated or
d) assembly of the nucleic acid partial sequences generated in the previous step.

1.2 D1 discloses methods for manipulating nucleic acids with the aid of arrays for, among other things, "assembling" of nucleic acids. Various possibilities for preparing nucleic acid fragments attached to the carrier are described, as is a synthesis reaction of a complementary nucleic acid strand by nucleotide components and an enzyme with a polymerase function followed by either further amplification cycles, which implicitly includes the detachment of the nucleic acids produced, or the "assembly" of partial sequences thus created into the desired nucleic acid sequence (page 2, line 12 - page 3, line 11; page 4, lines 7-18; page 8, lines 1-18; page 9, line 32 - page 10, line 27; page 13, line 22 - page 16, line 24; page 22, line 6 - page 23, line 20; figures 8-11). Use of the nucleic acids thereby produced for

diagnostic purposes or as part of a vector is also described (page 30, lines 3-16; page 12, lines 20-21).

The subject matter of claims 1-25 and 27-31 is therefore not novel over D1 (PCT Article 33(2)).

1.3 D2 discloses methods for manufacturing a plurality of different nucleic acids by providing a "microarray" laden with different nucleic acid fragments, followed by a hybridisation and amplification step according to the PCR principle involving supplying nucleotide components and an enzyme having a polymerase function, and the detachment of the nucleic acids produced ([16-18],[34],[36],[38],[39],[43-45],[84]). The use of the nucleic acids thereby produced for therapeutic and diagnostic purposes is also described ([30]). The subject matter of the independent claims 1, 3-7 and 9-30 is therefore not novel over D2 (PCT Article 33(2)).

1.4 Document D3 describes a method in which arrays with single-stranded DNA molecules are prepared which, once they have formed a "hairpin", are filled out with nucleotide components and enzyme in a synthesis reaction to nucleic acid double strands. In a further step, the double-stranded nucleic acids are detached from the array by a restriction enzyme (abstract; page 217, section 4 - page 219, section 2, figures 1, 7). The subject matter of claims 1, 9-11, 15, 16, 20-23, 29, 30 is therefore prejudiced as to novelty by D3 (PCT

Article 33(2)).

1.5 D4 discloses methods for amplifying nucleic acids wherein nucleic acids immobilised on a carrier are multiplied using the PR-PCR (reverse transcription polymerase chain reaction) principle. For this purpose, a carrier laden with different nucleic acid fragments is made available and a polymerase chain reaction is carried out in the presence of nucleotide components and recombinant thermostable polymerase, which implies the step of detachment and making available the previously made nucleic acid strands as in claim 1(c) (page 2, lines 4-22; page 6, line 20 - page 10, line 23). Use of this method for diagnostic and pharmacological purposes is also described (page 3, lines 1-2).
The subject matter of claims 1, 3-38 is therefore not novel over D4 (PCT Article 33(2)).

1.6 D5 discloses methods for manufacturing different synthetic nucleic acids by providing a substrate with different single-stranded nucleic acid fragments, which are made by supplying nucleotide components and an enzyme with polymerase activity complementary to the nucleic acid strand fixed to the substrate and are detached from the matrix strand by a denaturing step. This procedure may be repeated in a cyclical manner (page 2, line 16 - page 3, line 26).
Consequently, the subject matter of claims 1 and 3-7, 9-25 is not novel over D5 (PCT Article 33(2)).

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

2. Further observations

2.1 Despite there being several cited documents which are prejudicial to novelty, no objection is raised at present on the grounds of lack of unity between the methods described in independent claims 1 and 2. An objection of this type may be raised, however, on entry into the regional phase before the EPO if no unified concept in the form of a special technical feature linking the subject matter of claims 1 and 2 can be identified.

2.2 Independent claims 1 and 2 are not worded in the two-part form according to PCT Rule 6.3(b). In the present case, the two-part formulation appears suitable. Therefore, the features known in combination with each other from the prior art belong within the preamble (PCT Rule 6.3(b)(i)) and the remaining features in the characterising portion (PCT Rule 6.3(b)(ii)).

2.3 The use of the terms "wie" [such as] and "gegebenfalls" [possibly] in claims 1, 2, 20, 30 and 31 leaves the reader in uncertainty over the meaning of the relevant technical features. This has the consequence that the definition of the subject matter of these claims is not clear (PCT Article 6).

Preferred embodiments or additional optional method steps should be formulated as independent

Box No. VIII Certain observations on the international application

claims (PCT Rule 6.4).

2.4 Claims 29 and 30 disclose process steps, but no purpose. The claim category should therefore be examined (PCT Article 6).

2.5 The description does not accord, as prescribed in PCT Rule 5.1(a)(iii), with the claims, since claims 26-30 doe not appear to be supported by the description.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/013131

Box No. VIII Certain observations on the international application